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December 20, 2002

Forwarded by e-mail December 20, 2002

Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. 02N-0417: Proposed Rule – Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not be Infringed. (Federal Register/Vol. 67, No. 206/Thursday, October 24, 2002)

I. FDA's Proposed Rule

Mylan Pharmaceuticals welcomes the opportunity to submit written comments on the Food and Drug Administrations ("FDA's") proposed rule addressing certain abuses which currently undermine the Drug Competition and Patent Term Restoration Act of 1984 (Hatch – Waxman Amendments) to the Federal Food, Drug and Cosmetic Act. Mylan appreciates President Bush's acknowledgement of the importance of generic drugs from the Rose Garden on October 21, 2002. In his speech, the President stated that generic drugs are "just as safe and effective" as their brand counterparts, and "generic drugs make American health care far more affordable." As President Bush surely does, Mylan recognizes the need for balance between innovation and competition and believes that both are possible through legislative and administrative changes to the current Hatch-Waxman Amendment. Importantly, the President observed that, "unfortunately the careful balance of [Hatch-Waxman] is being undermined."

While the current proposal, and the President's acceptance of it, is a step toward affordable healthcare for all Americans, we must not lose sight of the need for legislation to accomplish the ultimate goal of affordable healthcare.

FDA's proposed rule effectively attempts to close some of the loopholes in Hatch-Waxman by:

1. Defining the types of patents that may be listed in the "Orange Book,"
2. Strengthening the declaration that patent holders must provide to "list their patents; and
3. Limiting NDA holders to a single 30-month stay.

While these are the issues at the heart of the abuses of the current system, one significant issue is not addressed in the proposed rule—the triggering of the 180-day exclusivity.

Department—Fax Numbers					
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The current system impairs a generic manufacturer's ability to 1) assess the risk involved with challenging patents that prohibit competition in the market place and 2) get timely FDA approval to market a generic product. Generics are thwarted from conducting these tasks because NDA holders are "incentivized" to list any and all patents in the Orange Book so that generics will be forced to challenge those patents, thus polluting a generic's ability to make an accurate risk assessment and invoking a 30 month period in which the FDA will not approve a generic ANDA.

It is in the interest of providers and consumers to change this current system whereby generic companies challenge inappropriately listed and unenforceable patents. However, the system needs to provide incentives and predictability to make the challenges feasible. Mylan applauds the intentions of the FDA and the President but strongly believes that due to the complexities of Hatch-Waxman it is unrealistic to look at any of the aforementioned issues in isolation.

In addition to the proposed changes contemplated in the FDA's proposed rule, combining legislative with administrative reform can better protect American consumers and healthcare providers. Specifically, Senate Bill 812, which passed the Senate in July 2002, approached the abuses of Hatch-Waxman through a comprehensive strategy of closing current loopholes in the system.

Accordingly, Senate Bill 812 provides an environment that allows timely access of generic drugs to consumers while preserving intellectual property rights and legitimate exclusivity for brand companies. The FDA and the Administration should recognize the value in embracing both the limited regulatory reforms contained in the proposed rule (with the revisions noted below) and the more comprehensive reform that is possible only through legislation.

II. Detailed Comments:

A. FDA's Proposal With Respect to Patent Listings and Patent Declarations

The FDA's proposed rule is described as clarifying the types of patents which may be appropriately listed in the Orange Book and revising the declaration that NDA applicants must provide to reflect this clarification. The proposed rule allows for drug substance (ingredient), drug product (formulation and composition), product-by-process and method-of-use patents to be listed in the Orange Book.

These patents are described in the proposal according to the following:

> For patents that claim the drug substance, the applicant shall submit information only on those patents that claim the drug substance that is the subject of the pending or approved application or that claim drug substance that is the same as the active ingredient that is the subject of the approved or pending application within the meaning of section 505(j)(2)(A)(ii), of the Act. For patents that claim a drug product, the applicant shall submit information only on those patents that claim a drug product that is the subject of a pending or approved application. For patents that claim a method of use, the applicant shall submit information only on those patents that claim indications or other conditions of use that are the subject of a pending or approved application. For approved applications, the applicant shall identify the indication or other condition of use in the approved labeling that corresponds to the listed patent and claim identified.

FDA's proposal explains that product-by-process patents and patents for a different form of a drug substance, as long as the drug substances are the "same" active ingredient under section 505(j)(2)(A)(ii), are appropriate for listing in the Orange Book.

FDA describes process, packaging, metabolite, and intermediate patents as not being permitted to be listed in the Orange Book according to its new rule. The FDA provides a sample Declaration, which the FDA feels encompasses the above-mentioned position on the types of patents that can be listed in the Orange Book by an NDA holder. However, FDA's proposed Declaration does not specifically exclude process, packaging, metabolite and intermediate patents, which could allow inappropriate patents to be listed.

B. Disadvantages of the FDA's Proposed Rules

While Mylan supports the position that the types of patents listed in the Orange Book by NDA holders needs curtailed, Mylan believes that a more restrictive stance than that proposed by the FDA is necessary. As an example, the FDA's proposal would allow NDA holders to list polymorph, hydrate and anhydrate patents in the Orange Book, regardless of whether the NDA holder's approved product is claimed by a listed patent. A posture such as this would promote situations whereby a non-patented form of a drug substance is being used by an ANDA applicant, yet the ANDA applicant will be sued for infringement of an Orange Book patent that is inapplicable to the NDA holder's product because such a suit is, in effect, a 30 month injunction against the ANDA holder. Mylan feels that situations such as the one described above must be eradicated and the only way to accomplish such is to not allow the listing of patents that claim a different form of a drug substance in the Orange Book.

Another example of potential abuse involves the FDA's proposal with respect to product-by-process patents. The agency has indicated that it will accept such patents for listing. However, wholesale listing of product-by-process patents would have a profound negative effect on generic drug approvals. Many NDA holders can be expected to take the position that any product-by-process patent that claims the approved product may be listed, irrespective of whether the process defined by the claim is actually used to manufacture the product. Thus, each process variation, whether or not commercially viable, potentially can lead to a product-by-process patent that would be listed in the Orange Book. Mylan proposes that only such patents in which the claims define the commercial process used to manufacture the approved product may be listed.

Finally, Mylan believes that the FDA proposed rule, although explicitly stating that there are several types of patents that should not be listed in the Orange Book, does not follow through with such prohibitions in the sample Declaration. It would be wise to expand and add exclusions to the Declaration. Further exclusions could include other forms of an active which are not the marketed form (i.e. acid, free base, salts, isomers), labeling matters (titration, dosing, registry, and business methods) and ornamental designs.

C. Mylan's Changes to FDA's Proposal Regarding Patent Listings and Declarations

As noted in section B above, Mylan supports the FDA's position in most instances except for its view on the form of a drug substance, product-by-process patents, labeling matters, and ornamental design issues. In order for the Declaration to work, the FDA will need to post the Declaration for public review and require an appropriate officer from the NDA holder to sign the Declaration attesting to its accuracy. Mylan believes that the following Declaration reflects Mylan's stance on allowing only the patents that should be listed into the Orange Book.

Patent Declaration Submission

This is a format for submission of patent information for NDAs submitted under section 505 of the Federal Food Drug and Cosmetic Act. For more detailed information please refer to 21 CFR 314.53 for NDA #_____

Time sensitive patent information pursuant to 21 CFR 314.53 for NDA#_____

The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

Trade Name:_____
Active Ingredient(s):_____
Strengths:_____
Dosage Form:_____
Approval Date:_____

A. This information should be provided for each individual Patent submitted.

1. US patent number:_____
2. Identify each claim which covers the drug substance or the drug product for which the applicant submitted the application or which covers a method of using such drug substance or product and can reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale of the drug_____
3. Expiration date_____(for patents whose terms have been extended pursuant to 35 U.S.C. § 156, the expiration date applicable to the product that has been approved or for which approval is sought should be identified)
4. Name of the Patent Owner:_____
5. US Agent (if patent owner or applicant does not reside or have place of business in the US)_____

B. For each claim identified in A2, please provide the following information:

1. The type of claim:
2. Drug Substance (Active Ingredient) _____Yes_____No
3. Drug Product (Composition/Formulation):_____Yes_____No
4. Method of Use:_____Yes_____No

C. For each Drug Substance claim identified, please provide the following information:

1. Is the active ingredient claimed in the patent the same physical and chemical form as the Drug Substance which is the subject of this NDA? Same physical and chemical form includes the polymorphic form(s) of the Drug Substance attributing to the drug's effectiveness; the salt, acid or free base form of the Drug Substance, only one of which can describe the Drug Substance; and the isomeric or enantiomeric form(s) and purity of the Drug Substance. Same physical and chemical form would not include metabolites and prodrugs of the Drug Substance.
_____YES_____NO
[*If the answer is "NO," stop here; the patent may not be listed in the Orange Book.*].
2. If YES, is the claim a product by process claim?_____YES_____NO
[*If the answer is "NO," please proceed to question 4.*].
3. If YES, is the Drug Substance made by the process described in the claim?
_____YES_____NO
[*If the answer is No stop here; the patent may not be listed in the Orange Book. If the answer is "YES" go to question 6].*
4. If NO, is the Drug Substance claimed in conjunction with packaging (i.e. a kit) or labeling limitations (i.e. a business method, registry, a new dosing/titration regime)? _____YES
_____NO

[*If the answer is "YES", stop here, the patent may not be listed in the Orange Book.*]
5. If NO, is the Drug Substance claimed in combination with another active ingredient or claimed as a method of using such a combination AND the combination is not the Drug Substance which is the subject of this NDA? _____YES _____NO
[If the answer is YES stop here; the patent may not be listed in the Orange Book.]
6. Statement of the basis for concluding why this claim meets 21 CFR 314.53

_____
_____
_____
_____
_____

D. For each Drug Product claim identified, please provide the following information:

1. Does the formulation or composition claimed in the patent cover the Drug Product which is the subject of this NDA?
_____YES _____NO
[*If the answer is "NO," stop here; the patent may not be listed in the Orange Book.*].
2. If YES, is the claim a product by process claim?_____YES_____NO
[*If the answer is "NO," please proceed to question 4.*].
3. If YES, is the Drug Product made by the process described in the claim??
_____YES_____NO
[*If the answer is "NO", stop here; the patent may not be listed in the Orange Book. If the answer is "YES" go to question 6].*
4. If NO, is the Drug Product claimed in conjunction with packaging (i.e. a kit); labeling (i.e. a business method, registry, a new dosing/titration regime); or ornamental design limitations?
[*If the answer is "YES", stop here, the patent may not be listed in the Orange Book.*].
5. If NO, is the Drug Product claimed in combination with another active ingredient or claimed as a method of using such a combination AND the combination is not the Drug Product which is the subject of this NDA? _____YES _____NO
[If the answer is YES stop here; the patent may not be listed in the Orange Book.]
6. Statement of the basis for concluding why this claim meets 21 CFR 314.53

_____
_____
_____
_____
_____

E. For each Method of Use claim identified, please provide the following information:

1. Is (a) an approved method of use of the approved drug product, or (b) a method of use of the approved drug product for which use approval is being sought, or (c) a method of use of the drug product for which use approval is being
sought claimed? Method of use refers to the "Indications and Usage" section of the Drug Product's label and not the other sections of that label._____YES ____NO
[*If the answer is "NO," stop here; the patent may not be listed in the Orange Book.*].

2. Statement of the basis for concluding why this claim meets 21 CFR 314.53

_____
_____
_____
_____
_____

The undersigned declares that all the above information have been provided in accordance with Title 28, Section 1746 entitled "Unsworn declarations under penalty of perjury".

Signed:_____

Date:_____

Title _____

Telephone Number_____

The undersigned also declares that for purposes of providing notice under ____, such notice can be sent to the NDA holder at the following name and address:

_____
_____
_____

and to the patent holder at the following name and address:

_____
_____
_____

D. 30- Month Stay

While a single 30-month stay could prevent the prevalent practice of "evergreening", such an approach could nonetheless, be subject to manipulation and abuse.

Even under the proposed rule, a patent owner / NDA holder could circumvent the intent of the proposed 30-month stay provision and further delay the proper introduction of generics to the market place. For example, a patent owner / NDA holder could bring a patent litigation alleging infringement of one listed patent, thus invoking the automatic 30-month stay, while electing to improperly postpone suing on a second patent until the expiration of the 30-month stay or generic market approval. This litigation strategy could potentially lead to the further delay of generics in the marketplace because of the risk inherent with launching a product during

litigation. This provision is an example of the FDA's administrative limitations, which we believe should be addressed by legislative reform.

Legislation would allow for a more comprehensive approach by simultaneously motivating brand companies to sue within 45 days to effectively resolve the intellectual property issues relating to the submission. Additionally, under the proposed legislation, if the brand elects not to sue within 45 days the generic company can file a declaratory judgment action on day 46. This reform would provide a balance which would accomplish the underlying goal of timely and predictable access of affordable drugs in the marketplace while allowing brand companies to preserve their proper intellectual property rights.

Accordingly, because the FDA proposed rule does not comprehensively eliminate these litigation loopholes, the FDA's current proposal relating to the one 30-month stay could actually lead to further abuse and delays within the system. Therefore, while we agree that the FDA can administratively limit the types of patents listed in the Orange Book and strengthen the declaration submitted by the NDA holder, it is with regret that we cannot support the proposed administrative change limiting the 30-month stay. Mylan will remain active in lobbying for legislative reform that will truly close the loopholes in Hatch-Waxman.

E. Additional Issues for Consideration

As previously mentioned, Mylan wants to take this opportunity to highlight ancillary issues that have a significant impact on a generic manufacturer's ability to timely market their drugs.

i. **180-day exclusivity** – The current system allows for the 180-day exclusivity for an ANDA to be triggered by a district court decision. This undermines a company's ability to capitalize on the benefit of receiving such exclusivity after exhaustive litigation due to the nature and complexities of the patent litigation process. In order to restore the feasibility of successful patent challenges, the triggering event must be tied to an unappealable decision. Mylan continues to support the idea of a generic company's having the choice to launch a product after a successful district court decision; however, a company should not loose its exclusivity if it chooses to not launch a product until after an appellate court decision. Again, this approach would maintain a pro-competitive marketplace while giving assurances to the generic industry that if they are successful in knocking down a patent preventing competition they will be able to recoup their costs through the 180-day exclusivity.

ii. **30 day listing deadline** - Although the issue of timely filing patent information in the Orange Book is not addressed in FDA's proposed rule, Mylan would like to take this opportunity to point out that there is a statute requiring the NDA/Patent holder to list patents in the Orange Book within 30 days of issuance, but that the FDA's current rules penalize late listing only with respect to ANDA's that were filed during the period that the

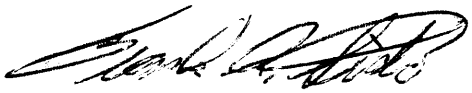
patent was not listed. The *statutory* penalty for non-compliance would be withdrawal of the NDA. Rather than implement this penalty and pull a reference-listed drug product from the market, the FDA does not require ANDA applicants with pending applications containing valid certifications to certify to a new patent listing in the Orange Book that is submitted more than 30 days after patent issuance. However, ANDAs filed after such a patent is listed in the Orange Book or pending ANDAs without valid certifications at the time of such a listing must provide certifications to such patent.

Mylan believes that the FDA needs a better mechanism with which to penalize NDA holders who do not list patents in the Orange Book within 30 days of issuance.

III. Conclusion

Mylan is very grateful for the President's and the FDA's public stance on the necessity of generic drugs in our marketplace. We hope that our comments are helpful and that we can move forward together in creating an environment of timely access of affordable prescription drugs for all Americans. Our country is in dire need for a solution to the unprecedented escalating costs of pharmaceutical drugs. The President's acceptance of generics being a part of the solution coupled with the FDA's proposed rule (as amended) and Hatch-Waxman reform is a step closer to affordable healthcare for our country.

Respectfully Submitted,



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